Standardization of Creatinine Measurement

NKDEP Manufacturers' Workshop

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Why Standardize Serum Creatinine Measurement?

To improve and normalize serum creatinine results used in prediction equations so that estimates of glomerular filtration rates (GFR) are accurate and comparable regardless of when or where tests are performed

Standardization is accomplished by establishing traceability to reference measurement procedures of higher order

Traceability (Standardization) requires…..

- Higher order Reference Measurement Procedures
  - *ISO 15193*
- Qualified Reference Materials
  - *ISO 15194*
- Suitable Reference Laboratories
  - *ISO 15195*

Traceability in Laboratory Medicine

International Standards

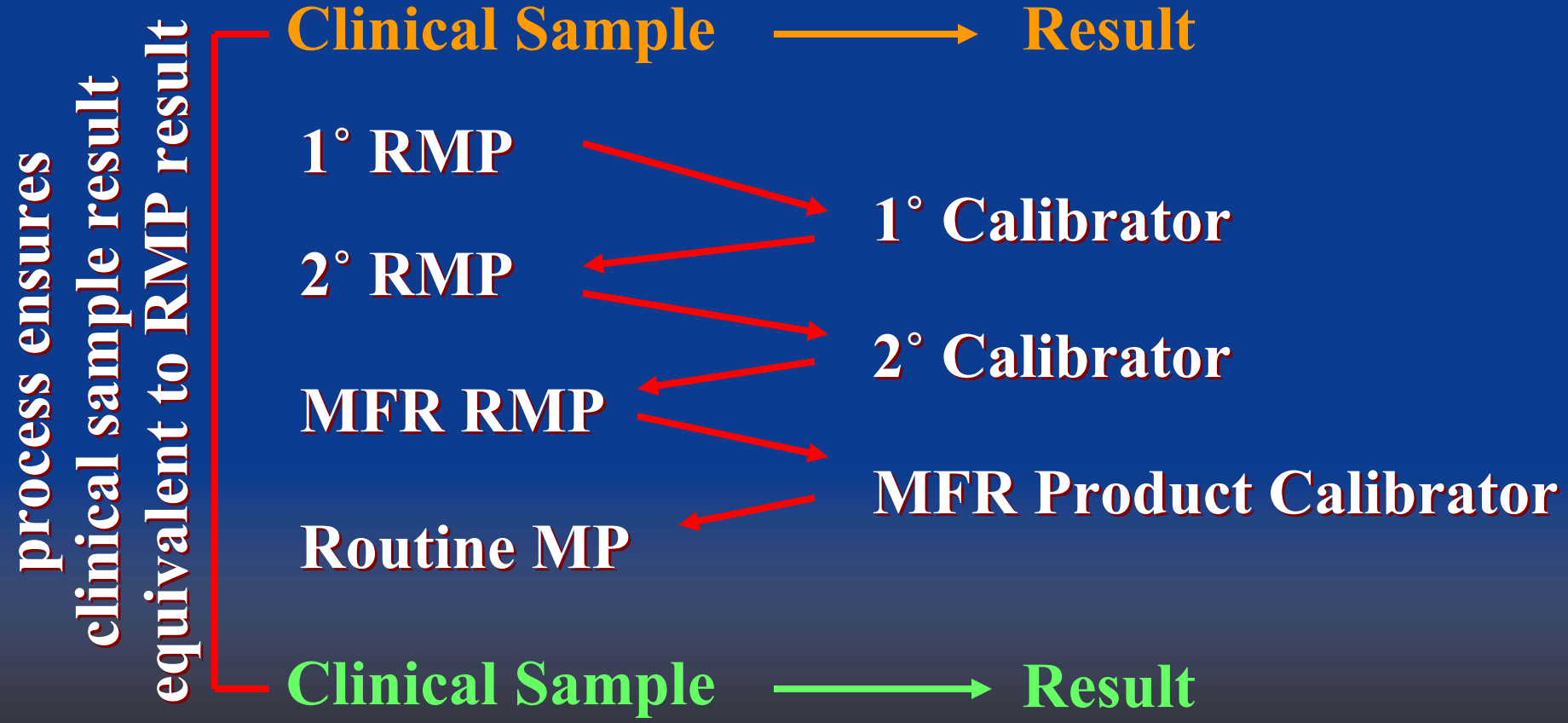
- Calibration and control materials

  ISO 17511

- Medical laboratories

  ISO 15189 & ISO 17025

Traceability in Laboratory Medicine



Joint Committee on Traceability in Laboratory Medicine

- Formed in June 2002
- Objective is to improve quality of healthcare through promotion of reference examination systems allowing traceability of examination results with improved comparability.
- Three main sponsors
  - IFCC (professionals in laboratory medicine)
  - BIPM/CIPM (professionals in metrology)
  - ILAC (professionals in accreditation)

Joint Committee on Traceability in Laboratory Medicine

- Two Working Groups formed
- Working Group 1 – Reference Materials & Procedures
  - Establish criteria for acceptance of materials and procedures and produce lists of such items

    (BIPM website at www1.bipm.org/en/committees/jc/jctlm)
- Working Group 2 – Reference Laboratories
  - Establish criteria for accreditation of reference laboratories at the calibration level, establish contacts to form networks, and promote parallel comparisons

Reference Materials Approved by JCTLM for Creatinine Measurement

Primary Reference Material

Name	Form		Available From
SRM 914a	crystalline creatinine	99.7±0.3 mass%	NIST[1]

[1] National Institute of Standards and Technology, Gaithersburg, MD

Reference Materials Approved by JCTLM for Creatinine Measurement

Secondary Reference Materials

Name	Form	Concentration Level	Available From
BCR 573	lyophilized serum	0.78±0.16 mg/dL	IRMM[1]
BCR 574	lyophilized serum	1.19±0.015 mg/dL	IRMM
BCR 575	lyophilized serum	4.57±0.08 mg/dL	IRMM
SRM 909b-1	lyophilized serum	0.64±0.006 mg/dL	NIST[2]
SRM 909b-2	lyophilized serum	5.29±0.061 md/dL	NIST

[1] Institute for Reference Materials and Measurements, Geel, Belgium
[2] National Institute of Standards and Technology, Gaithersburg, MD

CAUTION!!

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The Secondary Reference Materials from IRMM and NIST have not been evaluated for commutability with field methods, therefore they may be unsuitable for use in assay calibration

Comparison of performance between the IRMM and NIST materials has not been performed, therefore interchange of materials for assessing trueness is not recommended

Creatinine Accuracy Calibration Verification/Linearity Survey

- Product designation: LN24
- Prepared from fresh-frozen serum
- Concentration range: 0.5 – 4.0 mg/dL
- Seven 1.0 ml specimens
- Creatinine values will be assigned for each concentration level in the Survey using a high-level reference method
- Suitable for assessing calibration of field methods
- Available: 4th quarter of 2004

Reference Measurement Procedures Approved by JCTLM for Creatinine Measurement

Method	Institution
ID-GC/MS	NIST, Gaithersburg, MD
ID-GC/MS	University of Ghent, Belgium
ID-GC/MS	DGKC, Bonn, Germany

Recommendations for Standardizing Creatinine Measurement

- Develop a reference material for serum creatinine with proven commutability with individual patient serum
- Develop a high level reference method with high throughput (e.g. LC/MS) that manufacturers can use to validate assay trueness
- Establish high level/high throughput reference method in several labs (including at least one US lab) capable of providing reference services with reasonable turnaround time and cost
- Introduce a fresh-frozen serum-based PT program (e.g. CAP new linearity survey) which is value assigned by a reference measurement procedure that manufacturers can use to assess calibration of field methods

Standardization does not correct for non-specificity problems. Non-specificity issues must be addressed by IVD manufacturers.